A Review of the State-of-the-Art Methods for non-Calcified Plaque Detection in Cardiac CT Angiography

Muhammad Moazzam Jawaid, Sanam Narejo, Imran Ali Qureshi, and Nasrullah Pirzada

***Abstract*—The non-invasive diagnosis for cardiac abnormalities has been turned into a reality in recent years. This is based on the fact that advanced imaging equipment can acquire sub-millimeter details of the internal organs. An important example is the use of state-of-the-art computed tomography (CT) as a substitute of conventional catheterization. It is interesting that calcium-based vascular deposits can be quickly identified in CT; however, non-calcified plaque detection remains a challenging task due to lower intensity values. In this context, a number of methods have been reported for efficient detection and segmentation of non-calcified plaques in recent years. In order to advance the existing knowledge and extend the operational efficiency in this domain, it is extremely important to review the state-of-the-art literature. Accordingly, we present a comprehensive review of non-calcified plaque detection method in this paper presents. We believe that this can serve as a starting point towards productive clinical research in this domain.**

***Index Terms*—Coronary segmentation, non-calcified plaques, plaque detection.**

I. Introduction

The main arterial network responsible for providing oxygenated blood to the heart muscles is termed as coronary tree. In this context, Coronary Heart Disease (CHD) refers to a state in which calcium, cholesterol and fatty materials are accumulated inside the coronary vasculature. The growth of these depositions (plaques) leads to obstruction of blood flow towards heart muscles. As a consequent, oxygen starved heart tissues began to die and result in fatal cardiac events including arrhythmias, heart failure and angina. Coronary heart disease has remained the leading death cause around the globe in 2013 with overall death toll of 8.14million as stated by fact sheet of the World Health Organization [1]. Likewise, the fact sheet issued by National Health Services (NHS), United Kingdom reveals that the annual death toll of coronary heart disease in United Kingdom is around 73,000, i.e. one casualty per seven minutes. The critical mortality level of CHD has drawn the interest of research community towards automated detection of coronary heart disease.

In a clinical context, early detection of coronary abnormalities can eventually help to minimize the casualties [2] by regulating minimizing the risk factors. In recent years, the advancements made in imaging industry have revolutionized the clinical diagnosis domain. The capability of imaging sub-millimeter based internal details made CTA a feasible alternative to cardiac cauterization for detecting coronary obstruction [3]; however, the composition of the coronary plaques pose a difficult challenge in the effective diagnosis.

The high intensity calcified plaques can be detected easily in CTA imagery [4]-[7]; however, the detection of the non-calcified plaques has been a challenging problem in clinical practice due to close proximity with blood voxel intensity. From the clinical point of view, the non-calcified plaques have been established as the most important indicator of acute coronary syndromes due to their fragile nature [8]. Moreover, unexpected rupture has made soft plaques much threatening, i.e. for many individuals, sudden death becomes the first sign of soft plaque in contrast to the calcified plaques which often lead to disease symptoms at early stages. In addition, the positive re-modeling associated with the soft plaques further amplifies the detection challenge as the radial stenosis detection based methods often miss the non-calcified plaques [4], [5], [9]-[11].

In context of automated detection of non-calcified plaques in CT, [6], [7], [12]-[14] had proposed different techniques; however, majority of the reported works employ manual interaction and validate results upon small data set to illustrate the proof of concept. Likewise, a number of plaque quantification algorithms [15]-[17] have been proposed in recent years with a motive of correlating CTA with intra-vascular ultrasound (IVUS) measurements; however, these methods again employ manual inputs in terms of the plaque position and length in respective coronary vasculature.

Hence, the intense focus of the current research is developing algorithms for early detection of non-calcified plaques to predict and avoid worst cardiac events [18]. It is evident that, to advance the existing knowledge, it is extremely important to investigate and review the shortcomings of current methods. Accordingly, we present in this paper a brief review for state-of-the-art methods in context of non-calcified coronary plaque detection.

II. Literature Review

For detection of the plaque affected segments, coronary arteries are examined for existence of fatty/lipid structures which decreases the flow of blood to cardiac muscles. It is important to mention that the pre-requisite for plaque detection is an efficient segmentation of coronary vasculature.

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The segmented vasculature is consequently investigated in context of the plaque detection. In this context, a comprehensive review of the vessel segmentation techniques and their associated features is presented by Lesage [19]. It can be observed in this section that all plaque detection methods start with vessel segmentation and subsequently compute the non-calcified plaque (if any).

A. Coronary Artery Extraction and Analysis for Detection of Soft Plaques in MDCT Images

1) Key Idea: The focus of this work [15] is detection of the non-calcified plaques in coronary arteries. Two CTA data sets have been evaluated for the plaques existence. The application of the proposed technique identifies the plaque location correctly in the coronary arteries and visual results are validated with statistical measures/graph data.

2) Methodology: This work presented a two-step methodology for plaque detection. After applying some pre-processing operations on the input image authors extracted the vessel centreline. In the first step authors obtained the centreline of the vessel in 3D volume by using technique proposed in [20] where vessel tracking phenomena is controlled by local eigenvalues of the Hessian matrix. To ensure the minimal impact of image local features on centreline extraction process, pre-processing is done to isolates those features like myocardial cavities and calcified plaques etc. In case of presence of calcified plaques (easily identifiable with high intensity) these calcified voxels are assigned low intensity value so that they should not disturb the vessel centreline.

Once centreline is generated, statistical modeling is used for lumen and arterial-wall segmentation. Gaussian mixture model is used to represent vessel and its surrounding tissues and then Expectation Maximization algorithm is employed to construct an optimized probability map. Due to the variations in the intensity values along the vessel, a cylindrical model based on the local neighborhood of centreline point is used with radius value equal to 10mm. This model extracts segment between two consecutive points of the vessel along with surrounding myocardium tissue. Extracted cylinder is modeled by three class Gaussian mixture model to obtain distribution parameters (i.e. Mean and Variance) for three classes namely vessel lumen, vessel wall and the Myocardium. After building probability map for three classes, lumen and vessel voxels are identified for each segment by investigating probability for every class.

3) Plaque Detection Phenomena: The existence of plaque is perceived by investigating geometric features of the vessel. The narrowing of the vessel is calculated by measuring the cross section area of the lumen A_L and wall A_W. Area for two consecutive points $P_{(i)}$ and $P_{(i+1)}$ is calculated as a ratio of (Volume/Length) between points. By contrasting the two area measures A_L and A_W, metric was obtained to indicate plaque presence as shown below in the Fig. 1. From a critical point of view, this is a computationally efficient procedure developed for uncovering soft plaques in CTA but no clinical validation of the results is discussed in the paper. Although author claims to detect the soft plaques but no detailed quantitative analysis of the detected plaques has been done. Another limitation of this method is that it requires bulk pre-and post-processing.

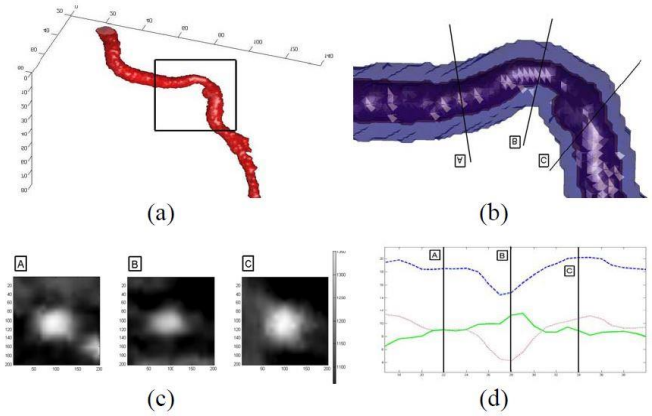


Fig. 1. Plaque detection process reproduced from [14]. (a) show 3D vessel structure, (c) shows three consecutive cross sections, (b) represent magnified view of the plaqued region and (d) represents lumen-vessel wall area statistics.

B. Soft Plaque Detection and Automatic Vessel Segmentation

1) Key Idea: This work [12] concentrates on the detection of the vulnerable lesions in coronary arteries. A total of 8 CTA data sets have been evaluated and 88% of non-calcified plaques in coronary arteries are detected with the help of proposed technique. Detected plaque locations are validated by expert clinicians as reported by the authors.

2) Methodology: This is a two-step procedure starting from segmentation of the arterial tree followed by the detection of the plaques. A unique characteristic of this technique is that it does not emphasize for any pre or post-processing of CTA data. Rather, simultaneous segmentations based upon localized information are the fundamental notion of this novel work. In the first stage arterial tree is segmented from volumetric data using universal modeling energy as the driving force of evolving contour as shown in Fig. 2. In the successive step two surfaces are constructed explicitly using morphological operations (erosion and dilation) such that they lie just inside and just outside the segmented vessel wall. Finally, two surfaces are evolved (outwards and inwards respectively) in simultaneous manner. Ideally these two segmentations must match each other at all points. Areas where these two curves do not match are identified as regions with non-calcified plaques. The process is illustrated with the help of figure below.

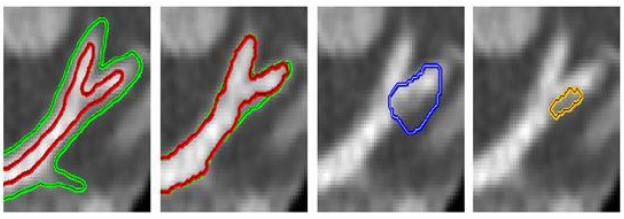


Fig. 2. 2D model for Plaque Detection Results on CTA imagery, reproduced from [12]. Red and green represents inner and outer surface. Blue represents ground-truth reference plaque and brown represents the detected plaque.

3) Driving Force for Segmentation: Segmentation of the arterial tree is the first step in detection of plaques. In this work segmentation of vessel is achieved using active contour model by posing it as an energy minimization problem. For vessel segmentation in the CTA volume, universal modeling

energy based on proposal of Chan and Vese [21] is used. Mathematical representation for universal modeling energy is given in equation 1. Here "I" represents input image and μ_{in}, μ_{out} represents mean intensity inside and outside the moving curve respectively. It is important to mention that localization is used during segmentation as it accommodates in-homogeneity caused by the varying intensity values along the length of vessel (Fig. 3).

$$Fum = \int_{\Omega_y} H\varnothing(y).\left(I(y) - \mu in(x)\right)^2 + \left(1 - H\varnothing(y)\right).\left(I(y) - \mu out(x)\right)^2 dy \quad (1)$$

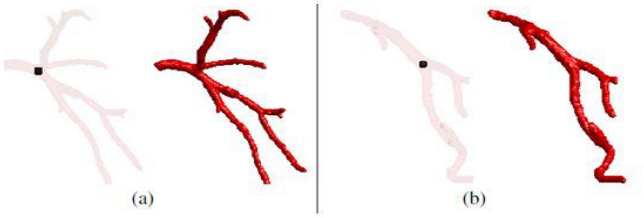


Fig. 3. Vessel Segmentation achieved using Universal Modeling energy/Chan-Vese model, reproduced from [5].

4) Plaque Detection Phenomena: Arterial Segmentation is followed by plaque detection where two explicit surfaces are initialized using morphological operation. These surfaces are initialized inside and outside the original segmentation so that non-calcified plaques that reside within the wall can be located between two surfaces. These explicitly generated contours are evolved by using Mean-Separation energy proposed by Yezzi *et al.* [22] that pulls two contours towards each other. By substituting the driving force into energy functional, contours evolves according to equation 2.

$$Fms = \int_{\Omega_y} \cdot \left(\frac{\left(I(y) - \mu out(x)\right)^2}{Aout(x)} - \frac{\left(I(y) - \mu in(x)\right)^2}{Ain(x)}\right) dy \quad (2)$$

Initially the local interior region of inside surface contains only the bright voxels, as the contour deforms it expands to capture more voxels containing blood but does not expand into a bit darker soft plaque voxels. Similarly external contour contains initially the Myocardium voxels, and it does not contract to accommodate the soft plaque voxels from the boundary. This way soft plaques can be isolated between two contours as neither will move into plaque voxels when driven by localized Means separation energy. Simply, in case of absence of soft plaque (no inhomogeneity in intensity values) these two evolving contours meet on the vessel wall, whereas deposition of the plaque inside wall will stop contours at the boundary of vessel and they will remain separate from each other. Fig. 2 and Fig. 4, shows 2D slices where the proposed method successfully isolates the soft plaques.

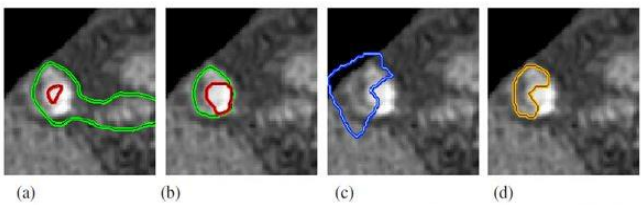


Fig. 4. 2D model for Plaque Detection Results on CTA imagery, reproduced from [12]. Red and green represents inner and outer surface. Blue represents ground-truth reference plaque and brown represents the detected plaque.

Before this work only [14] has attempted this research question; however their approach had several limitations. It requires substantial pre and post-processing of the volume data. Another concern is that no clue was provided for treatment of branching and bifurcation points. In contrast, this technique casts the problem in a variational active contour framework that operates directly on the raw imagery. So it naturally handles branching vessels and benefits from the geometric properties of active contours. However, this method requires smart initialization of two surfaces for successful detection of plaque. Failure to do intelligent initialization leads to under/over segmentation of non-calcified plaque.

C. Computerized Detection of non-Calcified Plaques in Oronary CT Angiography: Evolution of Topological Soft Gradient Pre-Screening Method and Luminal Analysis

1) Key Idea: Main focus of this work [7] is the detection of the soft plaques from CTA coronary vessels. Data of 83 patients was collected for analysis that contains a total of 120 soft plaques. A dedicated pre-screening algorithm is developed to minimize the false positives. Accordingly authors report a sensitivity of 92.5%.

2) Methodology: This is a multi-stage process where the detection of coronary arteries is followed by a series of geometric analysis. Focus of the research is designing pre-screening filter that optimizes the plaque detection process and reduces the false positives. Initial segmentation of arterial tress (shown in Fig. 5) is achieved by using algorithm MSCAR-RBG proposed by [23]. The used algorithms extracts about 86% correct arteries when compared with standard 17 segment coronary artery model, and the incorrect arterial branches are eliminated/inserted interactively, to ensure that accurate coronary arteries are to be passed to plaque detection phase.

By applying curve planer reformation, different branches of the arterial tree are transformed into straightened volume as it offers detailed analysis including diameter variations, wall behavior and surrounding tissues. In the following step, 81 * 81 rectangular 2D cross sectional planes are extracted across the length of the vessel branch. Interpolation process is used to obtain the voxel values falling on the orthogonal planes. Anisotropic diffusion is applied to minimize the impact of noise inducted because of motion and numerical resampling in CPR volume.

Fig. 5. Extracted Left and Right Arterial tree for extraction of NCP candidate Voxels, reproduced from [7].

After filtration, localized cylindrical analysis is performed for analyzing wall and lumen in detail by treating the vessel centreline as cylindrical axis. At every centerline point horizontal intensity gradient from the centreline to the vessel periphery is calculated in slice and location of the maximum radial gradient is treated vessel wall or the radius of the lumen

(It is assumed that all the voxels inside the vessel will have similar values giving a small gradient so vessel wall can be identified with large gradient shift). Radius for every point of the centreline is obtained and a Radius Profile is constructed that defines the vessel wall. Pre-Screening of candidates with Topological Soft Gradient A novel approach named topological soft gradient (TSG) is proposed for prescreening of NCP candidates along the vessel centreline. Fig. 6 represents the schematic layout for TSG method.

For TSG, gradient along the radial direction from vessel centreline to the outward wall is defined as: (average ct value at half radius from vessel centre to the vessel wall) - (average ct value at half radius from vessel wall to outwards). After obtaining the radial gradient at all locations of wall, 2-D surface characterizing the radial gradient field on the vessel wall is constructed. This radial gradient field is treated as 2D image and it is inspected to identify the regions having soft gradients as follows. A running window of 1.5 mm centered at each voxel of the centreline is defined and used to map corresponding values from gradient field. Histogram is generated for mapped values and upper boundary of lowest quartile is selected as soft gradient value for that particular centreline point. Successively obtained soft gradient values along the vessel centreline forms the soft gradient profile for the vessel. The soft gradient profile is traversed for local minima and every local minimum is labeled as NCP candidate and a 2mm vessel segment centered at the candidate voxel is defined as ROI for luminal analysis.

3) Plaque Detection Phenomena: Plaque related voxels are detected from NCP candidate voxels via quantitative analysis. Both geometric features and gray level characteristics are weighed in this step as geometric features corroborate the shape information and gray level values confirm the voxel intensity information. Intensity value statistics are obtained from CPR whereas for geometric features, two additional transformations are applied on the CPR volume namely Volumetric shape Indexing (VSI) and Gradient direction mapping (GDM). Volumetric shape Indexing to capture intuitive notion of local shape of surface, and Gradient direction mapping to characterize the local direction of gradient vector.

Four measures including mean, standard deviation and skewness are calculated for each voxel in all three transformed volumes. In addition, one geometric measure termed as radius differential is obtained by calculating the first derivative of the radius along the vessel. In total, 13 statistical measures are used for detecting existence of the soft plaques in the coronary arteries. According to the authors, reposted sensitivity of this TSG based method is 92.5%. Fig. 6 shows the detected plaque by applying the proposed method.

D. Automatic Transfer Function Specification for Visual Emphasis Coronary Artery Plaque

1) Key Idea: The main focus of this work [24] is to develop automatic transfer function capable of highlighting the pathological changes in the arteries that leads to clear visualization of soft plaques inside vessels. The direct volume rendering (DVR) represents vascular structures more realistically [25], hence automated transfer function can aid accurate interpretation in DVR. A total of 63 CTA datasets were evaluated in this work and detected soft plaques are in correspondence with expert's manual identification.

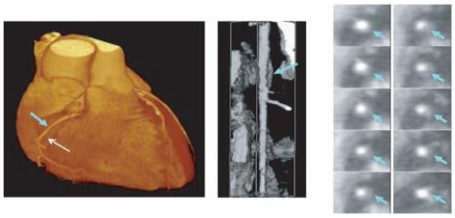


Fig. 6. Plaque identified by applying TSG pre-screening method, reproduced from [7].

2) Methodology: As soft plaques reside inside vessel walls and the HU (intensity-value) difference is insufficient to discriminate them from blood or cardiac muscles, it becomes difficult to identify the existing lesions. Transfer function (TF) are developed in this work, which helps clinicians to identify and track the vulnerable plaque present in the arteries. The main emphasis of this work is to improve the unique appearance of the clogged area for better visual analysis. Novelty in this work is TF based mapping of CT values to color and opacity that ensures different color coding for every dataset. This can incorporate the inconsistent diffusion of contrast agent in different patients. In contrast to traditional methods of highlighting the vessel lumen, vessel wall is focused in this work.

Coronary arteries constitute approximately 2.5 % of the total CTA volumetric data, so global histogram cannot represent the vascular behavior and pathological changes. Therefore segmentation is achieved in first step to focus on the region of interest. In this study, coronary arteries are delineated using method proposed in [26] and the under/over segmented coronaries are adjusted manually under the guidance of expert. Local histogram analysis is applied to approximate the blood intensity distribution (Mean and Variance) in the segmented arterial tree. Blood intensity values are estimated with Gaussian distribution and an optimal fit to the intensity distribution to the local histogram is calculated (using least squares). Blood Intensity parameters (μ, σ) were obtained as (μ_{blood} = 356+-136) & (σ_{blood} = 46+-16). This indicates that the average intensity varies strongly for different data sets, so setting a static threshold for hard plaques applicable to all data sets [27], [28] is not feasible. Threshold value (350Hu) defined by [29] shows an over estimation in the hard plaque separation. Accordingly authors define a new threshold for separating hard plaques as given in Equation (3).

$$T = \mu_{(blood)} + 3\sigma_{(blood)} \quad (3)$$

Vessel branches are analyzed individually with the help of arterial centreline. Intensity profile volume (IPV) is generated for every branch by processing centreline voxels. For each centreline point, (n) rays perpendicular to the centreline are casted in outwards direction. These rays are sampled in dataset up to radius (3mm to ensure that whole arterial cross section is covered, since 2.5 mm is maximum radius of coronary arteries). The sampled intensity values are stored in a slice of IPV as shown in Fig. 7, and this process is repeated for all centreline voxels of the branch.

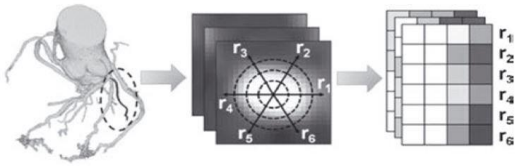


Fig. 7. Intensity profile volume generation for a vessel branch, reproduced from [24].

After building IPV, vessel wall intensities are detected. Vessel wall intensity is expected to be a vertical structure since all the values at a particular distance makes vertical line. A slice wise search mechanism is employed for locating vertical structures in IPV; however, these vertical structures are sometimes distorted because of artery remodeling which can be improved by applying Laplacian of Gaussian filter. So intensity distribution parameters (μ, σ) are obtained for every branch as shown in Fig. 8. Finally, the longest centreline branch satisfying the condition $(\mu_{wall}) < (\mu_{blood} - 2\sigma_{blood})$ is extracted as best candidate for global vessel wall approximation.

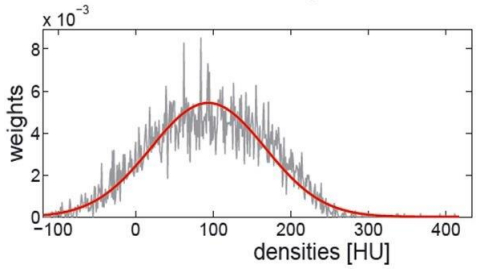
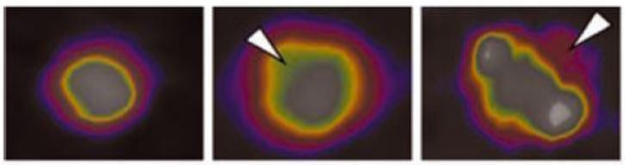


Fig. 8. Estimation of Vessel Wall intensity distribution for a vessel segment.

3) Plaque Detection Phenomena: Transfer function emphasizing the visualization of pathological changes is based upon supporting points which requires approximation of vessel wall intensity and blood intensity i.e. $(\mu_{wall}, \sigma_{wall}, \mu_{blood}, \sigma_{blood})$. Supporting points are related with different opacities and colors and intermediate values are linearly interpolated. Color association to the supporting points targets high contrasts for the vessel wall visualization. For the vessel wall, a color scale from blue over red to green is applied, yielding high contrasts for the visualization of different vessel wall intensities and thus different plaque deposits as illustrated in Fig. 9.



(a) (b) (c)

Fig. 9. Visualization enhancing the pathological changes in vessel. (a) without plaques (b) greenish color denser structures (c) Pinkish colour soft plaque.

TABLE I: DATA DESCRIPTION

Name	Description of dataset
A	Unvarified plaque candidates from angio set
N130	Unvarified plaque candidates from native set
N200	Unvarified plaques candidates from native set but highly calcified
V	Varified plaques

E. Automatic Detection of Calcified Coronary Plaques in Computer Tomography Datasets

1) Key Idea: The main focus in this work [9] is to design an automated framework for detection of calcified coronary plaques in CT images. In contrast to the avant-garde, both native and angio data sets are processed in this technique and this dual information is used for detection and assessment of calcified plaques. Authors report the success rate of the proposed method as 85%. The study only focuses on the calcified plaques; NCPs are not addressed explicitly in this work. (Table I).

2) Methodology: The proposed method is divided into 6 steps. First stage is the localization of aorta that leads to the segmentation of the coronary arterial tree. After extracting coronary artery, the potential plaque candidates based on Hu (defined threshold) values are identified. In order to eliminate false positives (included because of CT artifacts) from the plaque candidates, correspondence between two scans is accomplished via registration process between angio and native datasets as shown in the Fig. 10. Finally rule based approach is used to maximize the sensitivity by reducing false positives. Throughout the pipeline, state of the plaque detection process at any stage is represented by four sets.

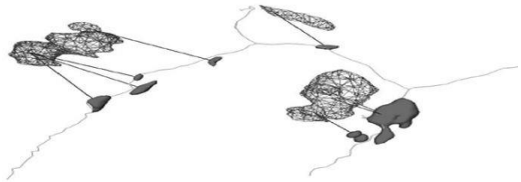


Fig. 10. Correspondence between Angio (solid) and native (mesh) plaque candidates.

3) Plaque Detection Phenomena: The ground truth for comparison of the obtained results is obtained with the help of a radiologist who marked the degree of the stenosis and the proximal and distal end positions of each plaque. Combination of native and angio data sets in the detection process achieves 85.5% detection rate according to the authors.

F. Automatic Segmentation of Coronary Arteries and Detection of Stenosis

1) Key Idea: The focus of this work [30] is to design a fully automated framework for identification of coronary artery plaques by highlighting the discontinuities in the vessel. The performance of the proposed approach achieves 97% success rate as reported by the authors. Authors did not specifically included or excluded the scope of NCPs.

2) Methodology: In the pre-processing step Input image is convolved with Gaussian filter to minimize possible CTA artifacts. After filtering, aorta is localized by applying connected component analysis. Vessel enhancement mechanism (Sobel operator) is applied to improve the connectedness between the branches of the coronary arteries and finally arteries are delineated by subtracting the localized aorta from the vessel enhance volume. Stenosis / calcification is detected by generating the centreline of segmented coronaries through skeletonization process.

3) Plaque Detection Phenomena: After generating the

skeleton discontinuities in the centreline are related with the stenosis as it symbolizes the presence of calcium/fats at corresponding location. The Intensity and diameter of the vessel at suspected points are evaluated and decision is made regarding degree of stenosis. Although the authors report 97% success rate of this approach but it is very limited and based upon several manually selected thresholds. Fig. 11 shows the detected stenosis points but no quantitative assessment has been done in this study. Along with this, the proposed method has not been tuned specifically for detecting soft plaques.

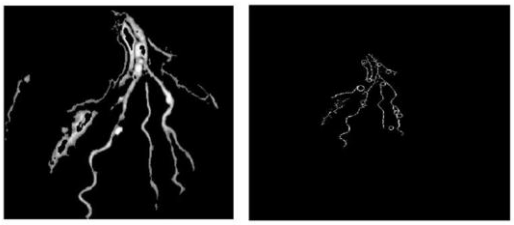


Fig. 11. Arterial tree with marked Plaque affected regions.

G. Measuring Non-Calcified Coronary Atherosclerotic Plaque Using Voxel Analysis with MDCT Angiography: A Pilot Clinical Study

1) Key Idea: The main focus of this work [6] is to design a voxel analysis approach for quantification of non-calcified plaque in coronary arteries. Quantification is performed in terms of diameter and volume of the plaque. Total 49 arterial cross sections (41 Normal and 8 abnormal with non-calcified plaque) are chosen from a set of 40 patient CTA data. According to the results voxel analysis technique appears to be robust method for measuring the vessel wall thickness, vulnerable plaques and resultant stenosis burden.

TABLE II: DATA DESCRIPTION

Total segments	Normal segments	Plaqued segments
Proximal right coronary	10	0
Left Main	4	1
Proximal left anterior descending	8	4
Mid left anterior descending	4	2
Proximal left circumflex	8	0

2) Methodology: Forty-one normal and eight abnormal arterial cross sections from six major arterial segments are chosen for analysis. Abnormal arterial cross section refers to non-calcified plaque holding planes where lesion did not occlude or narrow the arterial lumen greater than 70%. The cine projection is chosen to maximize the visual appearance and avoid the shortening or overlapping of branches. Specification for data used in the research is given in Table II.

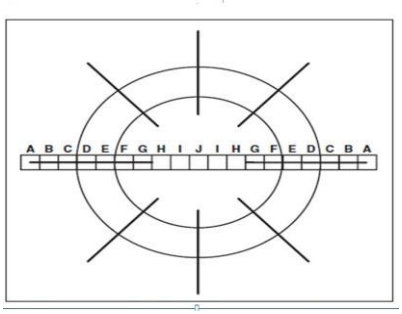


Fig. 12. Passing radial lines across wall to record intensity values.

Voxel Analysis is performed by plotting 8 radial lines at 45^o in the arterial cross sections. Each line starts from epicardial fat and terminates inside lumen to ensure that the wall surface has been tracked as shown in Fig. 12. For every line CT attenuation value is measured for seven (7) voxels starting from the epicardial fat representation (A, B) followed by interface of epicardial fat and vessel wall (voxel C), followed by voxels (D, E) representing the wall itself shadowed by (F, G) that represents the inner lumen. Plaque detection / identification mechanism can be visualized in Fig. 16 where the attenuation values for plane passing at line3 (having plaque inside wall) are plotted. The density of wall voxel (E=66) is less than normal segment.

In this study a total of 2296 voxel intensity values (41planes * 8lines * 7voxels) for normal arterial sections are logged. 448 voxel intensity values (8planes * 8lines * 7voxels) for plaqued arterial sections are recorded and the statistical analysis is perform for validating the presence of plaque.

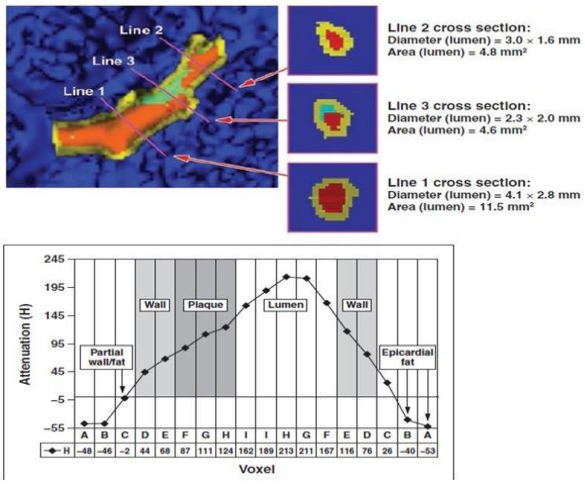


Fig. 13. Intensity value tracking for radial line voxels, and plaque detection reproduced from [31].

3) Plaque Detection Phenomena: As shown in the Fig. 13-14, the mean attenuation values of voxels (E-G) are significantly lower than their counterparts in the normal sections, indicating the presence of lower density structure (non-calcified plaque) compared with higher-density material (contrast medium and blood) in the normal cross sections.

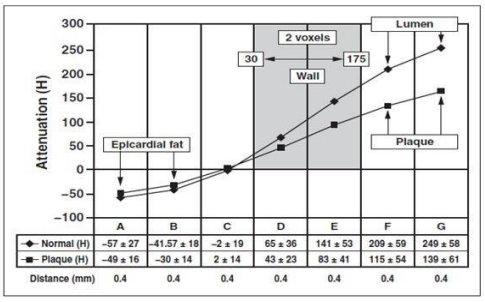


Fig. 14. Mean Intensity values for voxels in normal and clogged arteries.

H. A Voxel-Map Quantitative Analysis Approach for Atherosclerotic non-Calcified Plaques of the Coronary Artery Tree

1) Key Idea: Main focus of this work [32] is to develop a quantitative analysis framework for detection and

quantification of soft plaques present in the coronary arteries. Test CTA data for this research is obtained in a controlled environment of medical centre.

2) Methodology: According to the literature [33], [34], a pixel having CT attenuation number greater than 160Hu is considered as first voxel of the lumen. Consequently all the lumen voxel are supposed to have value greater than 160 whereas the external voxels are assumed to have intensity value less than 160. This cut-off value is used to delineate all the lumen voxels with the help of region growing algorithm. This segmented coronary artery mask is applied on the original CTA volume to extract the coronary tree model that retains all the original HU CT values for arteries whereas the surrounding structures are suppressed. Using a proprietary software Amira (v.5.4) skeleton/centreline is generated that is used in the detection stage. Voxel map is generated by applying morphological operations dilation and erosion. Dilation reflects the voxel changes outwards (boundary layers are termed as B1, B2, B3) whereas erosion mirrors voxel changes inside lumen (boundary layers are termed as B-1, B-2, B-3). Fig. 15(a) represents a cross sectional plane and intersecting the arteries orthogonally, and (b) shows a more localized view.

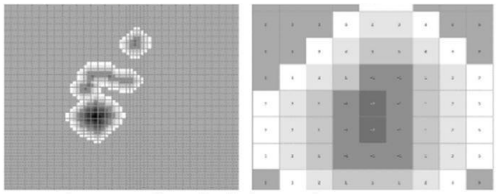


Fig. 15. Voxel map after dilation and erosion.

After generation of voxel map (dilation and erosion is done), the vessel wall (from outer border of lumen to the outer border of wall) is divided into four layers namely -1, 1, 2, 3. The attenuation values on the wall are divided into 6 groups to define the severity of the plaque composition and assigned different colors. These distinct colors are associated for better visual experience.

3) Plaque Detection Phenomena: The Inner lumen intensity value increases sharply as approaches close to the aorta; that is generally due to more concentration of the contrast agent whereas the CT value remains stable for boundary of vessel wall adjacent to lumen as shown in figure below. Afterwards, change in Hu values (gradient) is recorded at four defined layers that shows that mean CT value decreases from inside to outside. The abnormal behavior of gradient is related with the existence of the plaque as illustrated in Fig. 16.

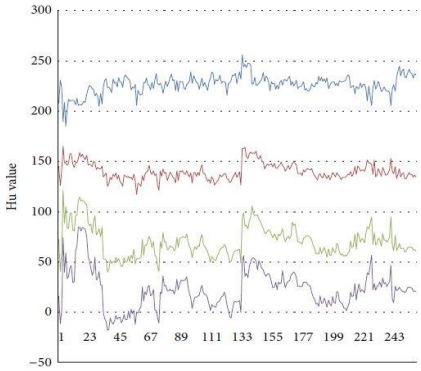


Fig. 16. The left figure shows Mean CT value of lumen voxels versus boundary voxels, whereas the Right graph shows Gradient of CT value at four layers of vessel wall from Inner lumen to outer vessel boundary.

I. Automatic Segmentation of Soft Plaque by Modelling the Partial Volume Problem in the Coronary Artery

1) Key Idea: The main theme of this work [35] is to tackle the partial volume problem in segmentation so that mis-classification of voxels is minimized during segmentation process. Authors reported some statistical analysis showing the effectiveness of this approach.

2) Methodology: Measuring small objects like coronary arteries in CTA volume is problematic task as it comprises of very small fraction of the whole data. Generally statistical or intensity thresholding based method are used for arterial segmentation that classifies voxels as vessel lumen or background. In contrast to the conventional delineation algorithms that make deterministic decision of assigning labels to voxels as vessel or background (although a voxel may belong to more than one structure at a time due to partial volume effect), this technique emphasizes the use of fuzzy algorithm based on Markov random field. Statistical methods reinforced with fuzzy algorithms can ensure high accuracy during assignment of a voxel to a particular class by incorporating the partial volume effect. By combining Markov random field model with Fuzzy K-means clustering, more accurate segmentation can be achieved. Although quantitative suggests that number of misclassified voxels are reduced but this approach requires the manual annotation of the region of interest on 2D slices for optimization.

J. Framework for Detection and Localization of Coronary non-Calcified Plaques in Cardiac CTA Using Mean Radial Profiles

1) Key Idea: Recently an efficient method has been proposed in [36] in which authors proposed the use of radial profiles for effective detection of non-calcified plaques. The main idea of the work is detection and localization of non-calcified coronary plaques.

2) Methodology: Starting with hybrid energy-based coronary tree segmentation [37], vertical radial profiles are computed around centre line for exploiting intensity variations. In the subsequent step, authors validated the use of computed radial profiles by associating non-calcified plaque intensities as illustrated in Fig. 17.

3) Plaque Detection Phenomena: Subsequently, the radial profiles are used to derive hand-crafted feature including moving deviation, mean, lumen intensity and radial variations as shown in Fig. 18. Finally, a SVM model is used for training

and testing over plaque affected coronary segments. In addition to plaque detection, authors proposed method for precise localization as well; however, the localization performance explicitly depends upon the detection algorithm. This limitation can lead to a number of false negatives i.e. small intensity dips may be missed in plaque localization method.

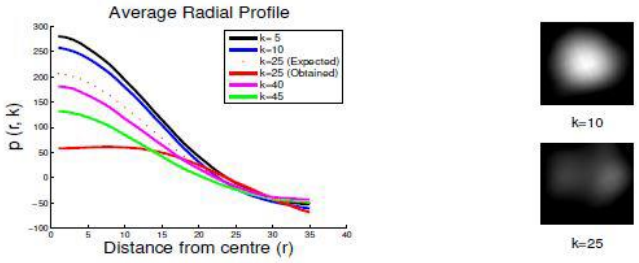


Fig. 17. Use of mean radial profile to exploit non-calcified plaque based intensity dips. Left shows intensity distribution for normal and abnormal cross sections, whereas right shows circular cross section.

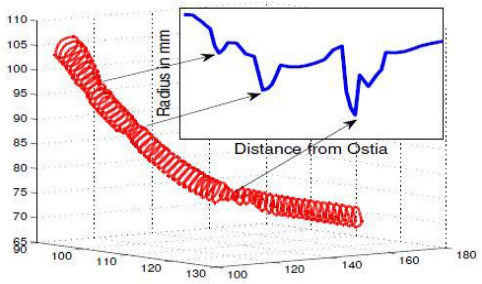


Fig. 18. Radial variations across the plaque affected sections in coronary vessel.

K. Machine Learning Based Anomaly Detection

In addition to above explained methods, a number of technique have been proposed in literature with a theme of computing CT based-plaque coronary plaque. An important method focusing on cross-section based vascular abnormality detection was proposed by Zuluaga *et al.* [27]. Based on the "density level detection" technique of Steinwart [38], authors employed an unsupervised learning approach in this work for detecting abnormal cross-section. In this method, the vascular cross-sectional images were discretely sampled around centreline to derive the feature set for suppressing outliers. Subsequently, they used an SVM model trained on normal cross sections to label the outliers (i.e. the cross sections which violate the intensity pattern of normal class) as abnormal. According to the reported results, a good detection rate of 79.62%, was reported for 9 clinical CTA datasets; however, the selection of anomaly concentration parameter _ plays an important role in overall results. In addition, a large number of normal cross-sections having similar intensity pattern are required for good training of SVM due to one-class nature of supervisor.

Another use of learning method was reported by Tessman [13], in which coronary stenosis effected cross-sections were detected. In the first step, the pre-extracted coronary centerline was used to map the vessel segment with a series of multi-scale overlapping cylinders to identify the sampling points inside the segment. Subsequently, image based features like intensity, gradient and the first-second order derivatives were extracted at the sampled points to identify high intensity calcifications. Moreover, global features including image mean, entropy and variance were used in combination with Haar-like features to detect the low intensity soft plaques. According to the reported results, the plaque detection accuracies were 94% and 79% respectively for two classes of plaques i.e. calcified and non-calcified. It should be noted that the low accuracy for non-calcified plaques illustrate that soft plaque detection demands a more sophisticated system i.e. beyond stenosis based computations to efficiently address vessel remodeling.

III. Conclusion

This paper presents a brief overview of the literature addressing detection, segmentation and quantification of the non-calcified plaques in cardiac CT angiography. We believe that this can serve as a starting point for researchers intended to work on new/automated plaque detection algorithms.

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